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Executive summary

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Executive summary

Objective

The objective of this assessment was to evaluate the effectiveness and cost-effectiveness of testing for hepatitis C virus (HCV) among former injecting drug users (IDUs).

Description of proposed service

Testing is defined as efforts to identify people with HCV infection and to offer them antibody and, if necessary, RNA testing, that is, systematic case-finding.

Case-finding for HCV may take place in a range of settings, using a variety of methods. This assessment examines a general case of systematic case-finding and explores the effectiveness and cost-effectiveness of case-finding in specific settings using a range of approaches: general practice, prisons and services for people who misuse drugs and alcohol. The population of interest is people who are former IDUs. In most, although not all, settings considered, the initial step in case-finding is the identification of this population group. In addition, two scenarios are considered in which testing is offered to whole populations: prison inmates and, according to age, people in contact with general practices.

HCV status is investigated using enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) testing. People with chronic HCV infection are considered for combination therapy using pegylated interferon and ribavirin in standard doses for 48 weeks. Treatment is offered without histological staging to people who are otherwise eligible and whose HCV infection is with genotypes 2 and 3. People with other genotypes (predominantly 1 and 4) are offered biopsy to assess the severity of liver damage. Cases with moderate to severe hepatitis are offered treatment, if otherwise eligible. Cases of mild hepatitis with genotypes 1 and 4 undergo monitoring, with subsequent treatment if the severity of hepatitis advances.

In order to consider potential benefits of case-finding other than antiviral combination therapy, the impact of offering brief interventions aimed at reducing the incidence of alcohol intake above prescribed limits is also examined.

Epidemiology and background

Hepatitis C is a blood-borne RNA virus which causes slowly progressive chronic liver disease. The most common viral genotypes in England are 1a (32%), 1b (15%) and 3a (37%). The virus is transmitted primarily as a result of contact with blood and blood products. Sharing of injecting paraphernalia among IDUs is currently the commonest route for infection. Sexual and vertical transmission may occur but are unusual.

Approximately 80% of people exposed to HCV will fail to clear the virus during the acute phase and will become chronically infected. Acute infection is usually asymptomatic. Chronic symptoms are non-specific and, in general, mild until progression of liver disease occurs.

The prevalence of HCV is thought to be around 0.4% in England and Wales. The majority of known cases in 2003 were aged <45 years old. A cohort study among new IDUs in London and Brighton (2001) suggests a high prevalence and rising incidence of HCV infection. The incidence of chronic infection in IDUs is around 40%, although some regional variation (33–57%) has been shown. The prevalence of former IDUs is uncertain and available estimates of 0.22–0.8% of the general population may underestimate the size of this population.

HCV infection impacts on quality of life, demonstrated using a wide range of health status measures. Fatigue is common in mild or moderate hepatitis and studies using the short form with 36 items (SF-36) have demonstrated effects on general health, vitality, emotional well-being and ability to undertake social roles.

Treatment for HCV infection has undergone substantial changes in the last decade with the establishment of pegylated interferon combination therapy as standard treatment in many countries. Sustained clearance of virus is achieved in up to 90% of recipients, although treatment is ▶

required for up to 48 weeks and is associated with reduced quality of life during that time.

Alcohol is an important determinant of progression of HCV disease, with increased consumption (over 50 g/day) being associated with a 60% increase in the relative risk of cirrhosis. About 40% of IDUs have high alcohol intake. Many studies have shown, in the general population, that brief counselling interventions are effective in reducing alcohol consumption.

Methods

A decision analytic model was developed to investigate the impact of case-finding and treatment on progression of HCV disease in a hypothetical cohort of 1000 people. This was compared with a cohort in whom no systematic case-finding is implemented but spontaneous presentation for testing is allowed to occur. A group of epidemiological and clinical experts informed the structure of the model, which has three main components: (1) testing and diagnosis, (2) treatment (3) long-term consequences of infection. A fourth component, case-finding strategies, examines the potential impact of case-finding in three settings: prisons, general practice and drug services.

The testing and diagnosis component of the model is a simple decision tree. Treatment is incorporated as part of a Markov model which represents the progression of HCV disease as transitions between discrete health states (mild, moderate or severe hepatitis; cirrhosis; decompensated cirrhosis; transplant and death).

Parameter estimates were obtained from literature searches, carried out on a range of electronic databases, and through contact with experts in the field. No methodological restrictions were applied, but searches were constrained to papers published or available in English.

Progression to cirrhosis was estimated from a meta-analysis of epidemiological studies. Other transition probabilities were obtained from literature review. Prevalences of risk factors for progression were obtained from a range of sources, including primary data from the Trent Regional Database Study. Data on costs and utilities of relevant health states were obtained from a recent trial of treatment for mild HCV disease. The effectiveness of combination therapy was estimated from a recent systematic review and meta-analysis. Effectiveness of brief interventions for alcohol reduction was obtained from a recent meta-analysis. Mortality from liver disease and other causes was estimated from routine UK mortality data.

Each cohort is assumed to be 37 years old at inception. The model runs for the lifetime of the cohort. Costs (base year 2004) and benefits [quality-adjusted life-years (QALYs)] were discounted at 6% and 1.5%, respectively.

Inherent uncertainty in the model was explored using extensive one-way sensitivity analyses, threshold analyses and probabilistic sensitivity analysis. A range of scenarios were explored using stochastic analyses. Value of information analysis was carried out to determine the value of further research.

Results

Case-finding for HCV is likely to prevent, for 1000 people approached, three cases of decompensated cirrhosis, three deaths due to HCV and one case of hepatocellular cancer (at 30 years). Twenty-five additional people are likely to undergo combination therapy as a result of initial case-finding. One liver transplant is likely to be prevented for 10,000 people included in case-finding.

Case-finding is likely to cost, in the general case, around £760,000 more than a policy of not case-finding. The total cost of either strategy is high and driven predominantly by the cost of treatment with combination therapy (the costs of long-term consequences are heavily discounted owing to the duration of the model). Systematically offering testing to 1000 people would cost around £70,000.

In terms of life-years gained, case-finding is likely to result in an additional life-year gained for an investment of £20,084. Taking impacts on quality of life into account gives an estimate for the cost–utility of case-finding as £16,514 per QALY.

The probabilistic sensitivity analysis shows that, if NHS policy makers view £30,000 per QALY as an acceptable return on investment, there is a 74% probability that case-finding for HCV would be considered cost-effective. At £20,000 per QALY, the probability that case-finding would be considered cost-effective is 64%.

The cost-effectiveness of case-finding in different settings is similar, although the absolute costs ▶

and benefits vary considerably. In all analyses, the probability of case-finding being considered cost-effective at a level of £30,000 per QALY was high. Case-finding in drug services is likely to be the most expensive, owing to the high prevalence of cases in the tested population. Correspondingly, benefits are highest for this strategy and cost-effectiveness is similar, in average terms, to the general case. Case-finding in general practice by offering testing to the whole population aged 30–54 years is, paradoxically, estimated to be the least expensive option. This is because, based on the only UK study of this approach, only a small number of people accept the offer of testing and HCV prevalence in this group is much higher than would be expected from the general population. This approach carries the theoretical advantage that it may reach people whose injecting drug career was many years previously and is not known to others. Two approaches to case-finding in prison were considered, based on the results of studies in Dartmoor and the Isle of Wight prisons. These differed substantially in the prevalence of cases identified in the tested populations. The analysis based on data from Dartmoor prison had the least favourable average cost-effectiveness of the strategies considered (£20,000 per QALY).

Subgroup analyses based on duration of infection show that case-finding is likely to be most cost-effective in people whose infection is more long-standing and who are consequently at greater risk of progression. In people who were infected more than 20 years previously, case-finding yields benefits at around £15,000 per QALY. The results are insensitive to many of the input parameters when these are varied across credible limits. In particular, the cost of the testing process does not impact significantly on the estimate of cost-effectiveness, mainly because a high proportion of the comparator cohort are expected to present for treatment during the course of the model and will undergo the same testing protocol. Treatment effectiveness was modelled using estimates from randomised controlled trials and lower rates of viral response may be seen in practice. However, estimates of cost-effectiveness remained below £30,000 for all levels of treatment effectiveness above 58% of those shown in the relevant trials.

The value of information analysis, based on assumptions that 10,000 people might be eligible for case-finding and that programmes would run for 15 years, suggests that the maximum value of further research into case-finding is in excess of £19 million. Partial expected value of perfect information (EVPI) analysis shows that the utility estimates used in the model eclipse all other factors in terms of importance to parameter uncertainty. This is not surprising, since the point estimates for differences in utility between states and across the arms of the model are small.

Implications for practice

Case-finding for HCV is already supported by national and international guidelines. The current assessment lends weight to these policies by demonstrating that case-finding is likely to be considered cost-effective when set alongside other potential uses of healthcare resources.

However, the estimated cost-effectiveness is not so favourable that all approaches could unequivocally be considered to represent good value for money. In particular, we have shown that strategies for case-finding that predominantly identify people early in the course of their disease may be less valuable than those which seek to identify those with more long-standing disease.

Although our findings suggest that case-finding is cost-effective, we have been unable, owing to the striking paucity of relevant data, to characterise with as much precision as we would like the configuration of real world approaches to case-finding.

Conclusions

Case-finding for hepatitis C is likely to be considered cost-effective by NHS commissioners. Although there remains considerable uncertainty, it appears unlikely that cost-effectiveness would exceed the levels considered acceptable.

Further improvements in the effectiveness of treatments to slow or halt disease progression are likely to improve the cost-effectiveness of case-finding.

Case-finding is likely to be most cost-effective if targeted at people whose HCV disease is probably more advanced.

Further empirical work is required to specify, in practice, different approaches to case-finding in appropriate settings and to evaluate their effectiveness and cost-effectiveness directly.

Further research

The following areas should be priorities for further research (in priority order):

1. Pilot studies of case-finding strategies are needed, in particular to develop methods of finding people who were infected decades ago and to evaluate uptake of testing, adherence and effectiveness of treatment.
2. Research into the benefits of case-finding followed by either treatment with combination therapy or approaches to behavioural modification which may result in benefits to infected and non-infected people who are currently injecting drugs.
3. Epidemiological research is needed to (a) monitor the scale and progress of the HCV epidemic and (b) estimate the number and type of IDUs across the UK in a wide range of settings in which case-finding might be considered.
4. Investigation of the effectiveness of harm reduction through advice to reduce alcohol intake in people with HCV is needed.
5. Research into the utility associated with disease states, treatment with combination therapy or counselling to achieve behavioural modification, and sustained viral response in current and former injecting drug users.
6. Studies on the effectiveness and cost-effectiveness of conventional and complementary treatment options such as low-dose pegylated interferon or dietary interventions, in terms of improving sustained viral response (SVR) rates and slowing disease progression.
7. Studies on the effect on SVR rates in former IDUs of using hepatitis nurse specialists (under the supervision of experienced consultants) in drug and alcohol units and prisons to improve treatment adherence.
8. Improved estimates of life expectancy in former IDUs.
9. Research into the knowledge and attitudes of clinicians and current and former IDUs towards HCV testing and treatment.
10. Studies on factors which may influence disease progression such as diabetes and obesity.

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 04/40/01. The contractual start date was in November 2004. The draft report began editorial review in June 2005 and was accepted for publication in September 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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